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Glucose tolerance abnormalities (GTA) in CF adults: a highly prevalent situation insight on potential mechanisms

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Introduction: GTA [impaired glucose tolerance (IGT) and CFRD] in CF patients is the most frequent co-morbidity and its prevalence increases with age. As life expectancy greatly increases over the last few decades, GTA has increased too. Screening of CF patients with an oral glucose test tolerance (OGTT) was implemented to establish prevalence of GTA and to provide some mechanistic explanations. The relative role of the two major mechanisms for diabetes occurrence (insulin secretion defect and insulin resistance) are highly debated in CFRD.
Methods: Ongoing study, CF patients without previous CFRD diagnosis and/or acute infection (stable clinical state for 4 weeks), are requested to have an OGTT. All tests were performed according to the standard recommendations. In order to evaluate insulin secretion and insulin sensitivity, glucose and insulin levels were measured at baseline and 30, 60, 90, 120 minutes post glucose load. Results are presented on 69 out of the 175 identified patients in our institution.
Results:

	Normal glucose tolerance (NGT)	IGT	CFRD
N (%)	44 (63,8)	18(26,1)	7(10,1)
Fasting glucose (mmol/L)	5,4 ± 0,4	5,6 ± 0,4	6,3 ± 1,0*
Stumvoll[1]	0,120 ± 0,021	0,104 ± 0,41$^{\Psi}$	0,117 ± 0,018
Insulin area under the curve[2]	4831 ± 2366	5884 ± 6297	3850 ± 1527

Insulin [1]resistance and [2]secretion index; *p < 0,01 compared to NGT and IGT; $^{\Psi}$p < 0,05 compared to NGT

Conclusion: GTA in a CF population without previous CFRD diagnosis are frequent (36%). Although insulin deficiency is believed to be the cause of these physiopathological process, our data showed that insulin resistance is also present in IGT and CFRD patients. Understanding glucose tolerance mechanisms will have an impact on the global CF outcomes.

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Glucose tolerance status in relation to lung function and growth

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Aims. To study (1) glucose tolerance (GT) status in relation to lung function (FEV_1%), nutritional status (weight sds) and linear growth (height sds); (2) changes in growth in the year preceding the diagnosis of impaired GT (IGT) and CFRD and (3) risk factors for IGT/CFRD.
Methods. The 73 CF patients who had an oral GT test in the preceding 18 months and 4 patients with CFRD diagnosed from fasting hyperglycaemia were studied. Clinical details at the time of the OGTT/diagnosis of CFRD and in the preceding year were obtained from the medical notes.
Results. Median age at the time of diagnosis of GT status did not differ but FEV_1%, weight sds and height sds were lower in patients with IGT and CFRD than in those with normal GT:

	Normal GT	IGT	CFRD	P
No. (%)	44 (57)	17 (22)	16 (21)	-
Median age (y)	13.9 y	14.8 y	14.5 y	0.2
Median FEV_1%	76%	58%	56%	0.003
Mean weight sds	-0.4 sds	-1.0 sds	-1.7 sds	0.009
Mean height sds	-0.5 sds	-1.3 sds	-1.4 sds	0.02

Changes in these clinical parameters in the preceding year did not differ significantly according to GT status. Patients who had a decline in weight and height >0.5 sds were not more likely to have a lower GT status (P=0.09 and 0.3). Gastrostomy feeds (P=0.03) and oral corticosteroid treatment (P=0.02) were risk factors associated with IGT and CFRD.
Conclusions. At diagnosis of IGT/CFRD, patients with CF aged 8-18 years at a tertiary centre had worse lung function, a poorer nutritional state and were shorter than patients with normal GT. However, poor weight gain and linear growth in the preceding year were not predictive of IGT/CFRD in individual patients. Patients who have gastrostomy feeds or who are on oral corticosteroids are at greater risk of IGT/CFRD, and should have OGTT prior to and at regular intervals during treatment.

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Serum Magnesium and Glucose Tolerance in Adults with CF

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Aims: Prospective studies have shown that low serum magnesium (Mg) increases the risk of type 2 diabetes. Adults with CF have a prevalence of diabetes far higher than the general population. We tested the association between serum Mg and dysglycaemia in British adults with CF.
Methods: Patients were identified through a CF clinic providing annual 75 g oral glucose tolerance tests (OGTT) to those without diabetes. Of 160 patients, we excluded 2 with incomplete data. We used ANOVA to test the difference in Mg levels between 3 groups defined by WHO criteria as normal glucose tolerance (NGT), impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), and diabetes. We evaluated the association between Mg and OGTT results among subjects without diabetes, and between Mg and haemoglobin A1c (HbA1c) for those with diabetes.
Results: Of 158 patients, 83 patients had NGT, 24 IGT or IFG, and 51diabetes. The mean for age was 26 (16-58) years, for BMI 21 (16–28) kg/m^2, and for Mg 0.82 (SD 0.09) mmol/l. The mean Mg differed between groups (p= 0.002) with values of 0.85, 0.81, and 0.79 mmol/l for NGT, IGT or IFG, and diabetes respectively. In patients without diabetes, Mg was inversely associated with both fasting plasma glucose and the 2 hour plasma glucose (β = -2.143, p = 0.019 and β = -1.061, p=0.019). These findings were not altered by adjustment for serum calcium, vitamin D levels, oral steroid use, days of IV antibiotic use in the previous year, pancreatin dose, or renal function estimated by Cockcroft Gault, none of which was associated with glucose levels. Among those with diabetes, we found no association between Mg and HbA1c.
Conclusions: In adults with CF, lower magnesium levels are associated with a higher risk of diabetes, and with higher glucose levels in the absence of diabetes. Prospective studies will better define these findings.

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Microvascular complications in patients with cystic fibrosis-related diabetes (CFRD)

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Aims This study aimed to quantitatively and qualitatively assess microvascular complications in CFRD, compared to diabetes mellitus type 1 (DM1). We hypothesized CFRD patients are less exposed to risk factors and therefore less prone to develop microvascular complications.
Methods 79 patients with CFRD were matched with 79 patients with DM1 according to sex, age, and duration of insulin therapy. The risk factors studied were: smoking, BMI, HbA1c, cholesterol, cholesterol/HDL ratio, and diastolic and systolic tension. Microvascular complications investigated were: retinopathy, peripheral neuropathy, nephropathy, and microalbuminuria.
Results In CFRD patients BMI (p<0.0001), smoking (p<0.0001), total cholesterol (p<0.0001), and HbA1c (p=0.056) were lower or not present, compared to DM1 patients. Cholesterol/HDL ratio and diastolic and systolic tension were similar in both groups.
The total number of complications was the same in both groups (23 cases). In the CFRD group the incidence of microalbuminuria (p=0.003) and the median albumin/creatinine ratio (p<0.0001) was higher, but retinopathy occurred more often in DM1 patients (p=0.04). No difference was found for peripheral neuropathy and nephropathy.
Conclusions The kind, but not the number, of microvascular diabetic complications, differed between CFRD patients and DM1 patients. Probably due to less exposure of CFRD patients to smoking, high body mass index, diastolic hypertension, high serum levels of HbA1c, and total cholesterol, they developed less retinopathy. The larger incidence of microalbuminuria is probably attributable to unidentified risk factors.